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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,492	03/06/2002	Elizabeth S. Light	142/003/PCT	8768

23874 7590 05/18/2006

VENTANA MEDICAL SYSTEMS, INC.
ATTENTION: LEGAL DEPARTMENT
1910 INNOVATION PARK DRIVE
TUCSON, AZ 85755

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,492	LIGHT ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7,17,19 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,17,19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments filed 2/17/06 have been entered. Claims 1, 3, 7, 17, 19, and 22 are pending. Claim 1 has been amended. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1, 3, 17, and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Nuovo et al. (Diagnostic Molecular Pathology 7(3): 158-163).

Nuovo et al. teach reagent that comprises a consensus probe cocktail that contains "multiple high HPV types" (page 160) and that detectably hybridizes to HPV types 16/18, 31, 33, 35, and 51, as well as to HPV types 39, 45, 52, 56, 58, 59, 68, and 70, but not to any of the low risk types tested (see Table 2). Regarding the requirement that the reagent comprise "a plurality of fragments having different nucleotide sequences" this requirement is inherently met by the fact that the reagent contains "multiple high HPV types" and at least some of these fragments detectably hybridise to each of the genomic types listed in the claims. Therefore the reagent taught by Nuovo et al. meets the limitations of the instant claims. Regarding claims17

and 19, the probe mixture would have inherently been contained in a container when it was provided, and indeed, during use the reaction vessel is a container that held the mixture.

Claim Rejections - 35 USC § 103

4. Claims 1, 3, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nuovo et al. (1995) in view of Cox et al. (Am. J. of Obstet. Gynecol., 1995, Vol. 172, p. 946-954).

Nuovo *et al.* teach a reagent for detecting human papillomavirus DNA in a cell sample comprising a plurality of genomic DNA probe sets, wherein each probe set comprises a plurality of nucleic acid fragments that detectably hybridize to essentially the entire full-length genomic sequence of HPV types 16 and 18, as well as a similar reagent that hybridizes to HPV types 31, 33, and 35. Nuovo *et al.* teach probe mixes provided by Digene that are made using the entire genome and that contain probes for these groups of HPV subtypes (p. 106, "Probe selection.").

With regard to claims 17 and 19, Nuovo *et al.* teach that they obtain these probes in kits from Digene Diagnostics, and these kits would inherently comprise containers containing the probes.

Nuovo et al. do not teach a reagent that comprises genomic probe sets that are fragments of essentially the full-length genomic sequence of all of the HPV types listed in claim 1.

Cox et al. teach a single reagent that comprises RNA probes to a group of high risk HPV types which includes types 16, 18, 31, 33, 35, 51, 45, 52, and 56 (p. 948). Cox et al. also teach separate assays to test for high risk HPV types 39 and 58 (p. 948), and suggest that the assay they used be expanded to include types 39 and 58 (p. 953, 2nd column).

It would have been prima facie obvious at the time the invention was made to have modified the reagents taught by Nuovo et al. so as to have provided a single reagent that includes nick-translated DNA probes to all of the types probed by Cox et al. One would have been motivated to provide such a mix in order to have provided a DNA probe cocktail that had the ability to detect many different known high risk HPV types in a hybridization assay analogous to that to that used by Cox et al. One would have been motivated to use DNA probes as opposed to RNA probes as taught by Cox et al. because DNA probes are more stable in solution than RNA probes which are more quickly degraded. With regard to the requirement that these probes "not detectably hybridize to the genomic sequence of a low-risk HPV type" this is considered to be a necessary property of the probe set taught by Nuovo et al. in view of Cox et al. since at very high stringency conditions such cross-hybridization would not be expected. Thus, in view of a secondary consideration, such as an unexpected result, the claimed invention is prima facie obvious.

With regard to claim 3, the cross-hybridization of the probes taught by Nuovo *et al.* in view of Cox et al. to the genomic sequences of HPV types 39, 45, 52, 56, 58, 59, 68, and 70 is an necessary property of the probe set. Some cross-hybridization of the full length probe cocktail taught by Nuovo *et al.* to these sequences could be expected under some stringency conditions. Notably, this is evidenced by the instant specification which teaches that full length nick translated genomic probe to HPV 18 hybridizes to 18, 39, 45, 56, 59, 68, and 70 and full length nick translated genomic probe to HPV 33 hybridizes to 16, 31, 33, 35, 45, 52, and 58.

5. Claims 7 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nuovo et al. in view of Cox et al. and further in view of in view of Bauer *et al.* (US 5639871).

The teachings of Nuovo et al. in view of Cox et al. are applied in this rejection as they were previously applied. These to not teach a reagent having probes in the concentrations given in claim 7. However, the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made, as is exemplified by Bauer *et al.* who teach "The optimal ration and concentration of probe fragments to be used in the hybridization are determined empirically (Col. 51, lines 60-63)."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52 ; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586 . Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372 ; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204 . However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433 ; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308 ; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314 . More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412 ; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213 ; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

For these reasons, the claimed invention is *prima facie* obvious.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 3, 7, 17, 19, and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 17-22 of copending Application No. 10/646633. Although the conflicting claims are not identical, they

are not patentably distinct from each other because given the totality of the teachings in claims 1-7 and 17-22 of the '633 application, it would have been prima facie obvious to one of ordinary skill in the art to have provided reagents comprising the sets of probes set forth in the rejected claims. For example, claim 5 of the conflicting application sets forth that the probes are full-length probes, and claim 7 sets forth the concentrations of the probes in the solution. Thus, the claims are rejected.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Remarks

The rejections in view of Miejer et al. under 102 and 103 are overcome by the amendment which requires that the probe sets comprise a plurality of nucleic acid fragments having different nucleotide sequences that detectably hybridize to a plurality of different sequences of each of the different HPV types. Miejer et al. teach cocktails which contain oligonucleotides having one nucleotide sequence for hybridization to each of the HPV types. A new 102 rejection is set forth to address the amendments to the claims.

The 103 rejection over Nuovo et al. in view of Cox et al. is maintained. Applicants traverse this rejection. Applicant points out the Nuovo et al. teach the use of the Omniprobe and wide spectrum cocktails that hybridize to both high risk and low risk types. However, a review of the rejection makes it clear that the examiner is not suggesting using these probe mixes, but instead is pointing to the reference for its teaching about high-risk specific probe cocktails. The reference must be considered in its totality for all that it teaches, including the high-risk specific

cocktails. Applicant also discusses deficiencies concerning the Oncor high risk probe kits. Again, these are not the probe kits relied upon in the rejection.

Regarding the Digene probes to either HPV 16 and 18 or HPV 31, 33, and 35, applicant points out that neither of these would detect all of the sequences required by independent claim 1. This is acknowledged in the rejection, and is the basis for the 103 rejection. Therefore, this analysis is an improper piecemeal analysis. Whether or not Nuovo would have known that these probe sets would have been capable of hybridizing to additional HPV types, this would still be an inherent or necessary property of the probe sets.

Applicant argues at the top of page 10 that the examiner uses improper hindsight reasoning to combine the references and that no teaching or suggestion to make the claimed combination is present in the prior art. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a clear statement of motivation was provided in the rejection. Further, In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge

gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Again, the reasoning to combine the references is based entirely upon the teachings in the prior art.

Applicants set forth that neither Nuovo et al. nor Cox et al. would have appreciated the benefits of using the claimed reagent comprising only six high-risk HPV probe sets. In response to applicant's argument that there is a different benefit of making this probe set (i.e. that it would detect a wide range of high risk HPV types), the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Further, the claims are not limited to a reagent that contains only the types listed in claim 1, since the claims are broadly drawn using "comprising language" and thus, any attempt to argue an unexpected result is not commensurate in scope with the claims.

Applicants further argues that one would not have known to substitute the RNA probes with DNA probes. However, the examiner does not make this suggestion, but instead simply suggests the modification of the teachings of Nuovo et al. so as to provide a single probe cocktail, similar to that taught by Cox et al. but for use in the method taught by Nuovo et al. Nuovo et al. provide genomic DNA probes to each of the HPV types recited in the claims, and the rejection suggests the combination of these DNA probes into a single cocktail, since a single cocktail of similar probes is taught by Cox et al., and for the benefit of using a single reagent instead of a series of different reagents.

The rejection is maintained.

The Double patenting rejections are maintained.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is

(571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

May 11, 2006